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FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE, SCISEARCH' ENTERED AT 20:21:46 ON 19 OCT 2001 4 S FELL (W) PROTEIN L1L2 492 S HYALURONATE (P) (BINDING (W) PROTEIN) L3 693 S L2 OR HABP L40 S L3 AND FELL L50 S L1 AND L3 158 S L3 AND CD44 L6 L7 3 S L6 AND PRECURSOR L8 0 S L3 AND ((CD44 (S) PRECURSOR)) L9 3 DUP REM L1 (1 DUPLICATE REMOVED) 104 DUP REM L6 (54 DUPLICATES REMOVED) L10 3 DUP REM L7 (0 DUPLICATES REMOVED) L11

STN updated

10/19/2001, EAST Version: 1.02.0008

Error ro Definition rs	ion	Overflow. Return string from Server is: 5.0.0.CD\$	w.string 1 rver 1 D\$
	Truncation Overflow. Return str from Serve	is: 5.0.0.CD\$	is: 5.0.0.CD\$
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Stamp	2001/10/1 9 20:44		2001/10/1 9 20:45
DBs		DERW	
Hits Search Text	L13 and CD\$\$		L13 and (CD44 adj precursor)
	4		0
	BRS L25		BRS L32
! ! 	5 BI		9 BE

File Cop7 09/466778 Upolated Search

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LOGINID:SSSPTA1600RXM
PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

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Web Page URLs for STN Seminar Schedule - N. America
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NEWS 3 Feb 06 Engineering Information Encompass files have new names
NEWS 4 Feb 16 TOXLINE no longer being updated
NEWS 5 Apr 23 Search Derwent WPINDEX by chemical structure
NEWS 6 Apr 23 PRE-1967 REFERENCES NOW SEARCHABLE IN CAPLUS AND CA
NEWS 7 May 07 DGENE Reload
NEWS 8 Jun 20 Published patent applications (A1) are now in USPATFULL
NEWS 9 JUL 13 New SDI alert frequency now available in Derwent's
                DWPI and DPCI
NEWS 10 Aug 23 In-process records and more frequent updates now in
                MEDLINE
NEWS 11 Aug 23 PAGE IMAGES FOR 1947-1966 RECORDS IN CAPLUS AND CA
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NEWS 13 Sep 17 IMSworld Pharmaceutical Company Directory name change
                to PHARMASEARCH
NEWS 14 Oct 09 Korean abstracts now included in Derwent World Patents
                Index
NEWS 15 Oct 09 Number of Derwent World Patents Index updates increased
NEWS 16 Oct 15 Calculated properties now in the REGISTRY/ZREGISTRY File
NEWS EXPRESS August 15 CURRENT WINDOWS VERSION IS V6.0c,
             CURRENT MACINTOSH VERSION IS V6.0 (ENG) AND V6.0J (JP),
             AND CURRENT DISCOVER FILE IS DATED 07 AUGUST 2001
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             CAS World Wide Web Site (general information)
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                                                 SINCE FILE
                                                               TOTAL
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FULL ESTIMATED COST
                                                      0.15
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FILE 'SCISEARCH' ENTERED AT 20:21:46 ON 19 OCT 2001
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=> s FELL (w) protein
            4 FELL (W) PROTEIN
=> s hyaluronate (p) (binding (w) protein)
          492 HYALURONATE (P) (BINDING (W) PROTEIN)
=> s L2 or HABP
         693 L2 OR HABP
⇒> s L3 and FELL
           0 L3 AND FELL
=> s L1 and L3
           0 L1 AND L3
=> s L3 and CD44
         158 L3 AND CD44
=> s L6 and precursor
            3 L6 AND PRECURSOR
=> s L3 and ((CD44 (s) precursor))
            0 L3 AND ((CD44 (S) PRECURSOR))
L8
=> dup rem L1
PROCESSING COMPLETED FOR L1
             3 DUP REM L1 (1 DUPLICATE REMOVED)
L9
=> dup rem L6
PROCESSING COMPLETED FOR L6
L10
           104 DUP REM L6 (54 DUPLICATES REMOVED)
=> dup rem L7
PROCESSING COMPLETED FOR L7
             3 DUP REM L7 (O DUPLICATES REMOVED)
L11
```

=> file biosis caplus embase medline scisearch

=> dis L9 1-3 ibib kwic

L9 ANSWER 1 OF 3 SCISEARCH COPYRIGHT 2001 ISI (R)

ACCESSION NUMBER: 95:22685 SCISEARCH

THE GENUINE ARTICLE: PY294

TITLE: THE DNA-ACTIVATED PROTEIN-KINASE IS REQUIRED FOR THE

PHOSPHORYLATION OF REPLICATION PROTEIN-A DURING

SIMIAN-VIRUS-40 DNA-REPLICATION

AUTHOR: BRUSH G S; ANDERSON C W; KELLY T J (Reprint)

CORPORATE SOURCE: JOHNS HOPKINS UNIV, SCH MED, DEPT MOLEC BIOL & GENET, BALTIMORE, MD, 21205 (Reprint); JOHNS HOPKINS UNIV, SCH

MED, DEPT MOLEC BIOL & GENET, BALTIMORE, MD, 21205; BROOKHAVEN NATL LAB, DEPT BIOL, UPTON, NY, 11973

COUNTRY OF AUTHOR: USA

SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE

UNITED STATES OF AMERICA, (20 DEC 1994) Vol. 91, No. 26,

pp. 12520-12524. ISSN: 0027-8424.

DOCUMENT TYPE: Article; Journal

FILE SEGMENT: LIFE LANGUAGE: ENGLISH

REFERENCE COUNT: 32

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB . . . during simian virus 40 DNA replication in vitro. To explore the functional significance of this modification, we purified a HeLa **fell protein** kinase that phosphorylates RPA in the

presence of single-stranded DNA. By several criteria we identified the purified enzyme as a. . .

L9 ANSWER 2 OF 3 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 1

ACCESSION NUMBER: 1980:230290 BIOSIS

DOCUMENT NUMBER: BA70:22786

TITLE: PANCREATIC SECRETORY RESPONSE TO CHOLECYSTOKININ

PANCREOZYMIN AND CAERULEIN IN THE CONSCIOUS RAT.

AUTHOR(S): LAUGIER R; PAPP A; DEMOL P; CHARBIT J-J; SARLES H

CORPORATE SOURCE: UNITE RECH. PATHOL. DIG. UNITE 31, INST. NATL. SANTE RECH.

MED., BLVD. DE LA GAYE, F-13009 MARSEILLE, FR.

SOURCE: PFLUEGERS ARCH EUR J PHYSIOL, (1980) 384 (1), 83-92.

CODEN: PFLABK. ISSN: 0031-6768.

FILE SEGMENT: BA; OLD LANGUAGE: English

AB. . . per h strongly inhibited volume flow and outputs of all the ions,

and the sum of the concentrations of anions fell.

**Protein** concentration and output increased with the same time course in response to both CCK and caerulein, i.e., a sustained stimulation.  $\cdot$ 

L9 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2001 ACS ACCESSION NUMBER: 1964:78523 CAPLUS

DOCUMENT NUMBER: 60:78523
ORIGINAL REFERENCE NO.: 60:13805c-e

TITLE: The effect of naphthaleneacetic acid and maleic

hydrazide on nitrogen metabolism of apricot flower

buds

AUTHOR(S): Udvardy, J.

SOURCE: Acta Botan. Acad. Sci. Hung. (1963), 9(3-4), 455-60

DOCUMENT TYPE: Journal LANGUAGE: English

AB Apricot flower buds following deep dormancy react to early warm periods with activated metabolism and thus become frost-susceptible. Treatments with naphthaleneacetic acid (I) and maleic hydrazide (II), known to delay bud growth, were studied. Buds of severed shoots were grouped: (1) stored

at 0.degree., or (2) subjected to a 3-stage (in 15 days) rise in temp. to 20.degree., (3) soaked before final temp. increase in I (1-200 mg./l.) for

0.5 hr. at 30.degree., or (4) in II (10-200 mg./l.). Changes in dry wt., N fractions, and sprouting follow. In (1), no change occurred. In (2), dry wt. decreased 50%, total N rose 23%, alc.-sol. N at first rose and then fell 50% below the control, sol. protein N rose 27%, and 95% of the buds swelled. In (3), 1-25 mg./l. allowed some increase in water uptake, total N rose 44%, sol. N fell, protein N rose, and bud growth was not reduced. With 100-200 mg./l., however, water uptake dropped 40% and total N 21%, sol. N rose 20% (synthesis inhibition), and protein N fell; buds were inhibited 69 and 80%. In (4), water uptake dropped 22-47%, total N fell 12-24%, sol. N rose 18-81%, and sol. protein N dropped 8-37% with inhibition of synthesis and probable proteolysis. Above 50 mg. II/l. no bud growth occurred.

## => dis L11 1-3 ibib kwic

L11 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2001 ACS ACCESSION NUMBER: 2000:457103 CAPLUS

DOCUMENT NUMBER: 133:103710

TITLE: Novel hyaluronan-binding proteins and encoding genes

INVENTOR(S): Hastings, Gregg A.; Liau, Gene; Tsifrina, Elena PATENT ASSIGNEE(S): Human Genome Sciences, Inc., USA; American Red Cross

SOURCE: PCT Int. Appl., 457 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

```
PATENT NO.
                 KIND DATE
                                        APPLICATION NO. DATE
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                         -----
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                   A1 20000706 WO 1999-US30462 19991220
    WO 2000039166
        W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ,
            DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS,
            JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK,
            MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ,
            TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ,
            MD, RU, TJ, TM
        RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
            DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
            CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                   A1 20011010
                                     EP 1999-964307
                                                       19991220
        R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, FI
PRIORITY APPLN. INFO.:
                                     US 1998-113871 P 19981223
```

AB The present invention relates to full-length WF-HABP, WF-HABP, OE-HABP, and BM-HABP, novel members of the hyaluronan receptor family. The invention provides isolated nucleic acid mols. encoding human to full-length WF-HABP, WF-

WO 1999-US30462 W 19991220

```
Full-length WF-HABP, WF-HABP, OE-HABP, and
     BM-HABP polypeptides are also provided, as are vectors, host
     cells and recombinant methods for producing the same. The invention
     further relates to screening methods for identifying agonists and
    antagonists of full-length WF-HABP, WF-HABP, OE-
    HABP, and BM-HABP receptor activity. Also provided are
    diagnostic methods for detecting disease states related to the aberrant
     expression of full-length WF-HABP, WF-HABP, OE-
     HABP, and BM-HABP receptors. Further provided are
     therapeutic methods for treating disease states including, but not
limited
     to, proliferative conditions, metastasis, inflammation, ischemia, host
     defense dysfunction, immune surveillance dysfunction, arthritis, multiple
     sclerosis, autoimmunity, immune dysfunction, and allergy.
IT
    CD44 (antigen)
     RL: ARG (Analytical reagent use); BPN (Biosynthetic preparation); BSU
     (Biological study, unclassified); PRP (Properties); PUR (Purification or
     recovery); THU (Therapeutic use); ANST (Analytical study); BIOL
     (Biological study); PREP (Preparation); USES (Uses)
        (BM-HABP; hyaluronan-binding proteins and encoding genes for
        screening agonists and antagonists for treating metastasis,
        inflammation, ischemia, allergy, etc.)
     CD44 (antigen)
     RL: ARG (Analytical reagent use); BPN (Biosynthetic preparation); BSU
     (Biological study, unclassified); PRP (Properties); PUR (Purification or
     recovery); THU (Therapeutic use); ANST (Analytical study); BIOL
     (Biological study); PREP (Preparation); USES (Uses)
        (OE-HABP; hyaluronan-binding proteins and encoding genes for
        screening agonists and antagonists for treating metastasis,
        inflammation, ischemia, allergy, etc.)
IT
     CD44 (antigen)
    RL: ARG (Analytical reagent use); BPN (Biosynthetic preparation); BSU
     (Biological study, unclassified); PRP (Properties); PUR (Purification or
     recovery); THU (Therapeutic use); ANST (Analytical study); BIOL
     (Biological study); PREP (Preparation); USES (Uses)
        (WF-HABP; hyaluronan-binding proteins and encoding genes for
        screening agonists and antagonists for treating metastasis,
        inflammation, ischemia, allergy, etc.)
     103715-96-4, Glycoprotein (chicken cartilage link precursor
ΙT
    protein moiety reduced)
                             202017-83-2 281684-73-9
     RL: PRP (Properties)
        (unclaimed protein sequence; novel hyaluronan-binding proteins and
        encoding genes)
L11 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER:
                         1993:189643 CAPLUS
DOCUMENT NUMBER:
                         118:189643
                         A novel secretory tumor necrosis factor-inducible
TITLE:
                         protein (TSG-6) is a member of the family of
                         hyaluronate binding proteins
                         , closely related to the adhesion receptor
                         CD44
                         Lee, Tae H.; Wisniewski, Hans Georg; Vilcek, Jan
AUTHOR(S):
                         Kaplan Cancer Cent., New York Univ., New York, NY,
CORPORATE SOURCE:
                         10016, USA
SOURCE:
                         J. Cell Biol. (1992), 116(2), 545-57
```

CODEN: JCLBA3; ISSN: 0021-9525

HABP, OE-HABP, and BM-HABP receptors.

DOCUMENT TYPE: Journal LANGUAGE: English

TI A novel secretory tumor necrosis factor-inducible protein (TSG-6) is a member of the family of **hyaluronate binding** 

proteins, closely related to the adhesion receptor CD44

AB TSG-6 cDNA was isolated by differential screening of a .lambda. cDNA library prepd. from tumor necrosis factor (TNF)-treated human diploid

FS-4

fibroblasts. The TSG-6 mRNA was not detectable in untreated cells, but became readily induced by TNF in normal human fibroblast lines and in peripheral blood mononuclear cells. In contrast, TSG-6 mRNA was undetectable in either control or TNF-treated human vascular endothelial cells and a variety of tumor-derived or virus-transformed cell lines.

The

sequence of full-length TSG-6 cDNA revealed one major open reading frame predicting a polypeptide of 277 amino acids, including a typical cleavable

signal peptide. The N-terminal half of the predicted TSG-6 protein sequence shows a significant homol. with a region implicated in hyaluronate binding, present in cartilage link protein, proteoglycan core proteins, and the adhesion receptor CD44. The most extensive sequence homol. exists between the predicted TSG-6 protein and CD44. Western blot anal. with an antiserum raised against a TSG-6 fusion protein detected a 39-kD glycoprotein in the supernatants of TNF-treated FS-4 cells and of cells transfected with TSG-6 cDNA. Binding of the TSG-6 protein to hyaluronate was demonstrated by copptn. Apparently, the inflammatory cytokine (TNF or IL-1)-inducible, secretory TSG-6 protein is a novel member of the family of hyaluronate binding proteins, possibly involved in cell-cell and cell-matrix interactions during inflammation and tumorigenesis.

ST tumor necrosis factor inducible protein hyaluronate; CD44 antigen monokine inducible protein

IT Antigens

RL: BIOL (Biological study)

(CD44, tumor necrosis factor-inducible secretory protein homol. to, of humans)

IT 145000-10-8, Glycoprotein TSG-6 (human clone .lambda.5 tumor necrosis factor-induced **precursor** protein moiety reduced) 145000-11-9, Glycoprotein TSG-6 (human clone .lambda.5 tumor necrosis factor-induced protein moiety reduced)
RL: PRP (Properties)

(amino acid sequence of, complete)

L11 ANSWER 3 OF 3 MEDLINE

ACCESSION NUMBER: 89156962 MEDLINE

DOCUMENT NUMBER: 89156962 PubMed ID: 2466108
TITLE: Glial hyaluronate-binding

protein in polar spongioblastoma.

AUTHOR: Bignami A; Adelman L S; Perides G; Dahl D

CORPORATE SOURCE: Department of Pathology, Harvard Medical School, Boston,

MA.

CONTRACT NUMBER: NS 13034 (NINDS)

SOURCE: JOURNAL OF NEUROPATHOLOGY AND EXPERIMENTAL NEUROLOGY,

(1989

Mar) 48 (2) 187-96.

Journal code: JBR; 2985192R. ISSN: 0022-3069.

PUB. COUNTRY: United States

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English Priority Journals FILE SEGMENT: ENTRY MONTH: 198904 Entered STN: 19900306 ENTRY DATE: Last Updated on STN: 19970203 Entered Medline: 19890407 TΤ Glial hyaluronate-binding protein in polar spongioblastoma. . . . well as reactive GFA protein-positive astrocytes were GHA AB protein-negative. We suggest that polar spongioblastoma derives from a GHA protein-positive glial precursor and pertinent to this suggestion is the observation that the periventricular germinal layer was found GHA protein-positive in a 22-week. Check Tags: Human; Male; Support, U.S. Gov't, Non-P.H.S.; Support, U.S. CTGov't, P.H.S. Antibodies, Monoclonal: DU, diagnostic use Antigens, CD44 \*Astrocytoma: ME, metabolism \*Brain Neoplasms: ME, metabolism \*Carrier Proteins: ME, metabolism Fetus: ME, metabolism Immunoblotting Middle Age \*Neuroglia:. 0 (Antibodies, Monoclonal); 0 (Antigens, CD44); 0 (Carrier Proteins) => dis L10 50-60 ibib kwic L10 ANSWER 50 OF 104 MEDLINE 93140194 ACCESSION NUMBER: MEDLINE PubMed ID: 7678658 DOCUMENT NUMBER: 93140194 Versican, a hyaluronate-binding proteoglycan of embryonal TITLE: precartilaginous mesenchyma, is mainly expressed postnatally in rat brain. AUTHOR: Bignami A; Perides G; Rahemtulla F CORPORATE SOURCE: Spinal Cord Injury Research Laboratory, Department of Veterans Affairs Medical Center, Boston, MA 02132. CONTRACT NUMBER: DE 08466 (NIDCR) NS 13034 (NINDS) JOURNAL OF NEUROSCIENCE RESEARCH, (1993 Jan) 34 (1) SOURCE: 97-106. Journal code: KAC; 7600111. ISSN: 0360-4012. PUB. COUNTRY: United States Journal; Article; (JOURNAL ARTICLE) LANGUAGE: English FILE SEGMENT: Priority Journals ENTRY MONTH: 199302 ENTRY DATE: Entered STN: 19930312 Last Updated on STN: 20000303 Entered Medline: 19930224

versican was identical to that previously reported for brain-specific

fibroblast proteoglycan, was studied in rat prenatal and postnatal development. In adult rat white matter and cerebellum, the distribution

The localization of versican, a large hyaluronate-binding

AB

of

glial hyaluronate-binding protein (GHAP). Versican was also found in gray matter where it formed characteristic coats around large neurons. It was also found. . . perineuronal coats were first observed on day 21 in the cerebral cortex. It is concluded that, with the exception of hyaluronate, brain extracellular matrix (ECM) is mainly produced postnatally and that the ECM protein produced by brain cells, most likely astrocytes,. Check Tags: Animal; Support, U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S. Animals, Newborn Antigens, CD44 \*Brain: ME, metabolism Carrier Proteins: ME, metabolism \*Cartilage: EM, embryology Fluorescent Antibody Technique Hyaluronic Acid: ME, metabolism Immunoblotting 0 (Antigens, CD44); 0 (Carrier Proteins); 0 (Proteochondroitin Sulfates); 0 (Receptors, Cell Surface) L10 ANSWER 51 OF 104 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 17 1993:647814 CAPLUS ACCESSION NUMBER: 119:247814 DOCUMENT NUMBER: A glycoprotein expressed by human fibrous astrocytes TITLE: is a hyaluronate-binding protein and a member of the CD44 family Da Cruz, L. A. G.; Cruz, T. F.; Moscarello, M. A. AUTHOR(S): Dep. Biochem., Hosp. Sick Child., Toronto, ON, M5G CORPORATE SOURCE: 1X8, Can. Cell Adhes. Commun. (1993), 1(1), 9-20 SOURCE: CODEN: CADCEF; ISSN: 1061-5385 DOCUMENT TYPE: Journal English LANGUAGE: A glycoprotein expressed by human fibrous astrocytes is a hyaluronate-binding protein and a member of the CD44 family The authors isolated and characterized an antigen from normal human brain AΒ called p80, which migrated with an Mr of 80 kDa on SDS PAGE. 80 kDa consists of a protein of about 55-60 kDa and carbohydrate (20-25 The carbohydrate is almost entirely of the N-linked type, although a amt. of O-linked carbohydrate was detected. Cross-reactivity with monoclonal antibodies A3D8 and A1G3 showed that p80 could therefore be considered an isoform of the CD44 adhesion mols. In addn., specific binding to hyaluronate which was not competed for by proteoglycan demonstrated that it involved different sites than the proteoglycan binding sites. Fucoidan and dextran sulfate increased the binding by 200-250% while chondroitin sulfate C also increased the binding but to a lesser extent. Heparin, heparan sulfate and chondroitin sulfates A and B did not have such an effect. The binding of p80 to hyaluronate was pH dependent with a max. at pH 6.4. Thus, p80 is an astrocyte-specific adhesion mol. glycoprotein p80 astrocyte hyaluronate CD44 antigen

```
IT
     Multiple sclerosis
        (glycoprotein p80 of fibrous astrocyte as hyaluronate-
        binding protein in relation to)
IT
     Glycoproteins, specific or class
     RL: BIOL (Biological study)
        (80,000-mol.-wt., as hyaluronate-binding
        protein, of fibrous astrocyte)
ΙT
     Antigens
     RL: BIOL (Biological study)
        (CD44, glycoprotein p80 as member of family of, of fibrous
        astrocyte)
ΙT
     Neuroglia
        (fibrous astroglia, glycoprotein p80 of, as hyaluronate-
        binding protein)
L10 ANSWER 52 OF 104
                          MEDLINE
ACCESSION NUMBER: 93016276
                                MEDITNE
DOCUMENT NUMBER:
                    93016276
                              PubMed ID: 1383238
TITLE:
                    Hyaluronan-binding protein in endothelial cell
                    morphogenesis.
                    Banerjee S D; Toole B P
AUTHOR:
CORPORATE SOURCE:
                    Department of Anatomy and Cellular Biology, Tufts
                    University School of Medicine, Boston, Massachusetts
02111.
CONTRACT NUMBER:
                    DE-05838 (NIDCR)
                    HD-23681 (NICHD)
SOURCE:
                    JOURNAL OF CELL BIOLOGY, (1992 Nov) 119 (3) 643-52.
                    Journal code: HMV; 0375356. ISSN: 0021-9525.
PUB. COUNTRY:
                    United States
                    Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:
                    English
FILE SEGMENT:
                    Priority Journals
ENTRY MONTH:
                    199211
ENTRY DATE:
                    Entered STN: 19930122
                    Last Updated on STN: 20000303
                    Entered Medline: 19921125
AΒ
      . . be involved in endothelial cell behavior. We have recently
     characterized a mAb, mAb IVd4, that recognizes and neutralizes HA-binding
     protein (HABP) from a wide variety of cell types from several
     different species (Banerjee, S. D., and B. P. Toole. 1991. Dev..
of
     their lamellipodia. Treatment with high concentrations of HA hexamer
     causes loss of immunoreactivity from these structures. We conclude that
     HABP recognized by mAb IVd4 is involved in endothelial cell
     migration and tubule formation.
     Check Tags: Animal; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
     Antibodies, Monoclonal
       Antigens, CD44
      Aorta
      Capillaries: PH, physiology
     Carrier Proteins: AN, analysis
     *Carrier Proteins: PH, physiology
      Cattle
      Cell Movement
     Cells, Cultured
    *Endothelium,. .
     0 (Antibodies, Monoclonal); 0 (Antigens, CD44); 0 (Carrier
CN
     Proteins); 0 (Oligosaccharides)
```

L10 ANSWER 53 OF 104 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 18

ACCESSION NUMBER: 1992:139093 BIOSIS

DOCUMENT NUMBER:

BA93:73318

TITLE:

A NOVEL SECRETORY TUMOR NECROSIS FACTOR-INDUCIBLE PROTEIN

TSG-6 IS A MEMBER OF THE FAMILY OF HYALURONATE

BINDING PROTEINS CLOSELY RELATED TO THE

ADHESION RECEPTOR CD44.

AUTHOR(S):

LEE T H; WISNIEWSKI H-G; VILCEK J

CORPORATE SOURCE:

DEP. MICROBIOL., N.Y. UNIV. MED. CENT., NEW YORK, N.Y.

10016.

SOURCE:

J CELL BIOL, (1992) 116 (2), 545-558.

CODEN: JCLBA3. ISSN: 0021-9525.

FILE SEGMENT:

BA; OLD

LANGUAGE:

English

A NOVEL SECRETORY TUMOR NECROSIS FACTOR-INDUCIBLE PROTEIN TSG-6 IS A MEMBER OF THE FAMILY OF HYALURONATE BINDING

PROTEINS CLOSELY RELATED TO THE ADHESION RECEPTOR CD44.

AB. . . signal peptide. The NH2-terminal half of the predicted TSG-6 protein

sequence shows a significant homology with a region implicated in hyaluronate binding, present in cartilage link protein, proteoglycan core proteins, and the adhesion receptor CD44. The most extensive sequence homology exists between the predicted TSG-6 protein and CD44. Western blot analysis with an antiserum raised against a TSG-6 fusion protein detected a 39-kD glycoprotein in the supernatants of TNF-treated FS-4 cells and of cells transfected with TSG-6

cDNA. Binding of the TSG-6 proteins to hyaluronate was demonstrated by coprecipitation. Our data indicate that the inflammatory cytokine (TNF or IL-1)-inducible, secretory TSG-6 protein is a novel member of the family of hyaluronate binding proteins, possibly involved in cell-cell and cell-matrix interactions during inflammation and tumorigenesis.

L10 ANSWER 54 OF 104 SCISEARCH COPYRIGHT 2001 ISI (R)

ACCESSION NUMBER: 92:313950 SCISEARCH

THE GENUINE ARTICLE: HU165

H-CAM EXPRESSION IN THE HUMAN NERVOUS-SYSTEM - EVIDENCE TITLE:

FOR A ROLE IN DIVERSE GLIAL INTERACTIONS

VOGEL H (Reprint); BUTCHER E C; PICKER L J AUTHOR:

CORPORATE SOURCE: STANFORD UNIV, MED CTR, SCH MED, DEPT PATHOL, STANFORD,

CA, 94305; VET ADM MED CTR, PALO ALTO, CA, 94304

COUNTRY OF AUTHOR:

SOURCE:

JOURNAL OF NEUROCYTOLOGY, (MAY 1992) Vol. 21, No. 5, pp.

363-373.

ISSN: 0300-4864.

DOCUMENT TYPE:

Article; Journal

FILE SEGMENT: LANGUAGE:

LIFE ENGLISH

REFERENCE COUNT: 47

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

H-CAM (CD44/Hermes antigen) is an 85-95 kDa AB

> widely-distributed cell surface adhesion molecule that participates in diverse cellular interactions. It is an important.

STP KeyWords Plus (R): CELL-ADHESION MOLECULES; HYALURONATE-

BINDING PROTEIN; LYMPHOCYTE HOMING RECEPTORS;

MONOCLONAL-ANTIBODIES; HUMAN-BRAIN; SURFACE GLYCOPROTEIN; WHITE MATTER;

## ANTIGEN; CD44; IDENTIFICATION

L10 ANSWER 55 OF 104 MEDLINE

ACCESSION NUMBER: 92316183 MEDLINE

DOCUMENT NUMBER: 92316183 PubMed ID: 1377637

TITLE: The extracellular matrix of rat spinal cord: a comparative

study on the localization of hyaluronic acid, glial

hyaluronate-binding protein,

and chondroitin sulfate proteoglycan.

AUTHOR: Bignami A; Asher R; Perides G

CORPORATE SOURCE: Department of Pathology, Harvard Medical School, Boston,

Massachusetts 02155.

CONTRACT NUMBER: NS 13034 (NINDS)

SOURCE: EXPERIMENTAL NEUROLOGY, (1992 Jul) 117 (1) 90-3.

Journal code: EQF; 0370712. ISSN: 0014-4886.

PUB. COUNTRY: United States

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199208

ENTRY DATE: Entered STN: 19920815

Last Updated on STN: 19960129 Entered Medline: 19920804

TI The extracellular matrix of rat spinal cord: a comparative study on the localization of hyaluronic acid, glial hyaluronate-

binding protein, and chondroitin sulfate proteoglycan.

AB The localization of hyaluronic acid (HA), glial hyaluronate-

binding protein (GHAP), and chondroitin sulfate (CS)

proteoglycan was compared in cryostat sections of rat spinal cord.  ${\rm HA}$ ,  ${\rm GHAP}$ , and  ${\rm CS}$  proteoglycan. . .

CT Check Tags: Animal; Comparative Study; Support, U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S.

## Antigens, CD44

\*Carrier Proteins: AN, analysis

\*Extracellular Matrix: UL, ultrastructure

\*Hyaluronic Acid: AN, analysis

Immune Sera

Immunohistochemistry

\*Nerve Tissue Proteins:.

hyaluronate-binding protein)

L10 ANSWER 56 OF 104 MEDLINE

ACCESSION NUMBER: 92303336 MEDLINE

DOCUMENT NUMBER: 92303336 PubMed ID: 1376955

TITLE: Some observations on the localization of hyaluronic acid

in

adult, newborn and embryonal rat brain.

AUTHOR: Bignami A; Asher R

CORPORATE SOURCE: Department of Pathology, Harvard Medical School, Boston,

Massachusetts.

CONTRACT NUMBER:

NS 13034 (NINDS)

SOURCE: INTERNATIONAL JOURNAL OF DEVELOPMENTAL NEUROSCIENCE,

(1992)

10 (1) 45-57.

Journal code: 126; 8401784. ISSN: 0736-5748.

PUB. COUNTRY: ENGLAND: United Kingdom

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Journal; Article; (JOURNAL ARTICLE)
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LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199207

ENTRY DATE: Entered STN: 19920731

Last Updated on STN: 19980206 Entered Medline: 19920722

AB . cryostat sections of brain and spinal cord obtained from adult, newborn and embryonal rat. The sections were incubated with glial hyaluronate-binding protein (GHAP) of human origin and the protein was visualized by indirect immunofluorescence with monoclonal antibodies raised to human GHAP and. . . glycoprotein, approximately 60,000 molecular weight, which is structurally related to the HA-binding region of cartilage ECM proteins. The distribution of hyaluronate in adult brain white matter and cerebellar cortex was similar to that previously reported for GHAP. In both cases, the reaction product formed a mesh surrounding myelinated axons and granule cells. Hyaluronate was also found in parts of the brain that did not contain GHAP. A finely reticulated mesh was observed in. . . large bulbar reticular neurons and dentate nucleus of cerebellum. The only part of the brain which appeared relatively free of hyaluronate was the molecular layer of the cerebellum. In newborn and embryonal rat, the densely packed cell bodies in cerebral gray matter, periventricular germinal layer and external granular layer of cerebellum were surrounded by hyaluronate. Small droplets of hyaluronate were observed in between the cylindrical epithelial cells lining the neural tube in 11 day embryos. Non-myelinated fiber tracts and the molecular layer of the developing cerebellum were relatively unstained. No hyaluronate was detected in the ependyma lining the cerebral ventricles and the central canal of the spinal cord.

CT Check Tags: Animal; Female; Support, U.S. Gov't, Non-P.H.S.; Support, U.S.

Gov't, P.H.S.

\*Animals, Newborn: ME, metabolism

Antigens, CD44

\*Brain: EM, embryology

\*Brain Chemistry: PH, physiology Carrier Proteins: ME, metabolism Cerebellar Cortex: ME, metabolism Cerebral Cortex: AH,. . .

CN 0 (Antigens, CD44); 0 (Carrier Proteins); EC 3.2.1.35 (Hyaluronoglucosaminidase)

L10 ANSWER 57 OF 104 MEDLINE

ACCESSION NUMBER: 91282778 MEDLINE

DOCUMENT NUMBER: 91282778 PubMed ID: 1711848

TITLE: Evidence for autophosphorylation of hyaluronate

binding protein and its enhanced
phosphorylation in rat histiocytoma.

AUTHOR: Babu B R; Gupta S; Datta K

CORPORATE SOURCE: Biochemistry Laboratory, School of Environmental Sciences

Jawaharlal Nehru University, New Delhi, India.

SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1991

Jun 28) 177 (3) 1291-8.

Journal code: 9Y8; 0372516. ISSN: 0006-291X.

PUB. COUNTRY: United States

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals ENTRY MONTH: 199107 ENTRY DATE: Entered STN: 19910818 Last Updated on STN: 19970203 Entered Medline: 19910731 Evidence for autophosphorylation of hyaluronate binding TIprotein and its enhanced phosphorylation in rat histiocytoma. AΒ This report documents for the first time the in vitro autophosphorylation of purified 68 kDa hyaluronate binding protein in presence of [32P] ATP. The rate of phosphorylation is proportional to the concentration of protein and to the time. . . western blot with antiphosphotyrosine antibodies, we have confirmed that the phosphorylation occurs at tyrosine residues. Immunoprecipitation with anti HA binding protein antibody shows a 5 fold increase in the phosphorylation in macrophage histiocytoma compared to normal macrophage. Supplementing hyaluronate with hyaluronate binding protein in the medium is further shown to enhance total protein phosphorylation in rat histiocytoma. Check Tags: Animal; Support, Non-U.S. Gov't \*Adenosine Triphosphate: ME, metabolism Antibodies Antigens, CD44 Carrier Proteins: IP, isolation & purification \*Carrier Proteins: ME, metabolism Cell Line Electrophoresis, Polyacrylamide Gel \*Fibroma: ME, metabolism CN 0 (Antibodies); 0 (Antigens, CD44); 0 (Carrier Proteins); 0 (Phosphates) L10 ANSWER 58 OF 104 MEDLINE ACCESSION NUMBER: 91154308 MEDITNE PubMed ID: 1705559 91154308 DOCUMENT NUMBER: Hyaluronan and a cell-associated hyaluronan binding TITLE: protein regulate the locomotion of ras-transformed cells. Turley E A; Austen L; Vandeligt K; Clary C AUTHOR: CORPORATE SOURCE: Department of Pediatrics, University of Manitoba, Winnipeg, Canada. SOURCE: JOURNAL OF CELL BIOLOGY, (1991 Mar) 112 (5) 1041-7. Journal code: HMV; 0375356. ISSN: 0021-9525. PUB. COUNTRY: United States Journal; Article; (JOURNAL ARTICLE) LANGUAGE: English FILE SEGMENT: Priority Journals ENTRY MONTH: 199104 ENTRY DATE: Entered STN: 19910428 Last Updated on STN: 19970203 Entered Medline: 19910408 Hyaluronan (HA) and one of its cell binding sites, fibroblast hyaluronan AΒ binding protein (HABP), is shown to contribute to the regulation of 10T1/2 cell locomotion that contain an EJ-ras-metallothionein (MT-1) hybrid gene. Promotion of. . . to stimulate locomotion back to the

original, acute rate, and the ability of an mAb specific to a 56-kD

fibroblast HABP to block locomotion. Further, both HA and HABP products are regulated by induction of the ras gene. The effect of exogenous HA is blocked by HABR, is dose-dependent. resides in its glycosaminoglycan chain. Uninduced cells are not affected by HA, HABR, or mAb and production of HA or HABP is not altered during the experimental period. These results suggest that ras-transformation activates an HA/HABP locomotory mechanism that forms part of an autocrine motility mechanism. Reliance of induced cells on HA/HABP for locomotion is transient and specific to the induced state. Check Tags: Support, Non-U.S. Gov't Antigens, CD44 \*Carrier Proteins: ME, metabolism Cell Line, Transformed \*Cell Movement \*Cell Transformation, Neoplastic Chondroitin Sulfates: PD, pharmacology Cloning, Molecular CN 0 (Antigens, CD44); 0 (Carrier Proteins) L10 ANSWER 59 OF 104 MEDLINE 91303851 ACCESSION NUMBER: MEDLINE PubMed ID: 1712867 DOCUMENT NUMBER: 91303851 Rapid assay of hyaluronic acid in serum. TITLE: Kondo T; Chichibu K; Usuki H; Matsuura T; Shichijo S; AUTHOR: Yokoyama M M Diagnostics Technology Labs, Chugai Pharmaceutical Co., CORPORATE SOURCE: Ltd., Tokyo. RINSHO BYORI. JAPANESE JOURNAL OF CLINICAL PATHOLOGY, SOURCE: (1991)May) 39 (5) 536-40. Journal code: KIV; 2984781R. ISSN: 0047-1860. PUB. COUNTRY: Japan Journal; Article; (JOURNAL ARTICLE) LANGUAGE: Japanese Priority Journals FILE SEGMENT: ENTRY MONTH: 199108 Entered STN: 19910908 ENTRY DATE: Last Updated on STN: 19960129 Entered Medline: 19910819 A method for measurement of hyaluronic acid (HA) level in serum was developed based on using "hyaluronic acid binding protein" (HABP )-coated polystyrene beads. After the beads and test serum being mixed, the mixture was incubated together with reaction buffer for 2 hours, and then the beads were washed. Subsequently, biotinylated HABP was added to the washed beads and incubated for 1 hour. Then peroxidase-conjugated avidin was added to the mixture and. Check Tags: Human Adult Aged Aged, 80 and over Antigens, CD44 Arthritis, Rheumatoid: BL, blood Carrier Proteins: DU, diagnostic use \*Hyaluronic Acid: BL, blood Methods

CT

AB

Middle Age

Osteoarthritis: BL,. 0 (Antigens, CD44); 0 (Carrier Proteins) CN L10 ANSWER 60 OF 104 MEDLINE 91311713 MEDLINE ACCESSION NUMBER: PubMed ID: 1713274 91311713 DOCUMENT NUMBER: Extracellular matrix of central nervous system white TITLE: matter: demonstration of an hyaluronate-protein complex. Asher R; Perides G; Vanderhaeghen J J; Bignami A AUTHOR: Department of Pathology, Harvard Medical School, Boston, CORPORATE SOURCE: Massachusetts. NS 13034 (NINDS) CONTRACT NUMBER: JOURNAL OF NEUROSCIENCE RESEARCH, (1991 Mar) 28 (3) SOURCE: 410-21. Journal code: KAC; 7600111. ISSN: 0360-4012. United States PUB. COUNTRY: Journal; Article; (JOURNAL ARTICLE) English LANGUAGE: Priority Journals FILE SEGMENT: 199108 ENTRY MONTH: Entered STN: 19910913 ENTRY DATE: Last Updated on STN: 19990129 Entered Medline: 19910829 Monoclonal antibodies were raised against human glial hyaluronate AB -binding protein (GHAP), a major CNS-specific glycoprotein known to bind hyaluronate in vitro. Frozen sections of dog and human spinal cord were digested with Streptomyces hyaluronidase in order to ascertain whether GHAP is bound to hyaluronate in vivo. Digestion with hyaluronidase, prior to staining of the sections by conventional indirect immunofluorescence, led to a drastic reduction. . Chondroitinase ABC (protease-free) was also effective in bringing about the release of GHAP from tissue sections. This enzyme also degrades hyaluronate. The effects of the chondroitinase were completely reversed by the addition of 1 mM Zn2+, a known inhibitor of this. Dog GHAP was isolated from spinal cord by means of ion exchange and affinity chromatography. This protein bound efficiently to hyaluronate in vitro. Dog and human GHAP had identical isoelectric points and similar peptide maps but different molecular weights. Dog GHAP (70 kD) was larger than its human counterpart (60 kD). These findings imply that GHAP exists in association with hyaluronate in CNS white matter. Immunoelectron microscopy revealed that GHAP fills the between myelin sheaths in dog spinal cord white matter. One is led to conclude therefore that an hyaluronate based extracellular matrix exists in CNS white matter. . . . Tags: Animal; Female; Human; Support, U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S. CT Amidohydrolases: PD, pharmacology Antibodies, Monoclonal: DU, diagnostic use Antigens, CD44 Biological Markers \*Carrier Proteins: AN, analysis Carrier Proteins: IM, immunology Cattle Chondroitin Lyases: PD, pharmacology \*Extracellular Matrix: CH,. . .

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0 (Antibodies, Monoclonal); 0 (Antigens, CD44); 0 (Biological
CN
     Markers); 0 (Carrier Proteins); EC 3.2.1.35 (Hyaluronoglucosaminidase);
EC
     3.5. (Amidohydrolases); EC 3.5.1.52 (peptide-N4-(N-acetyl-beta-
     glucosaminyl)asparagine amidase); EC 4.2.2.- (Chondroitin Lyases)
=> dis his
     (FILE 'HOME' ENTERED AT 20:21:00 ON 19 OCT 2001)
     FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE, SCISEARCH' ENTERED AT 20:21:46 ON
     19 OCT 2001
              4 S FELL (W) PROTEIN
L1
            492 S HYALURONATE (P) (BINDING (W) PROTEIN)
L2
L3
            693 S L2 OR HABP
L4
              0 S L3 AND FELL
L5
              0 S L1 AND L3
L6
            158 S L3 AND CD44
L7
              3 S L6 AND PRECURSOR
r_8
              0 S L3 AND ((CD44 (S) PRECURSOR))
              3 DUP REM L1 (1 DUPLICATE REMOVED)
L9
            104 DUP REM L6 (54 DUPLICATES REMOVED)
L10
              3 DUP REM L7 (0 DUPLICATES REMOVED)
L11
=> log off y
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US-CL-CURRENT: 536/23.5,536/24.31

US-PAT-NO: 6025138

DOCUMENT-IDENTIFIER: US 6025138 A

TITLE: Method for detecting the presence of a polynucleotide encoding a hyaluronan receptor expressed in human umbilical vein endothelial cells

DATE-ISSUED: February 15, 2000 INVENTOR-INFORMATION:

CITY STATE ZIP CODE COUNTRY NAME. N/A N/A Hawkins; Phillip R. Mountain View CA CA N/A N/A Sunnyvale Wilde; Craig G. Los Altos Hills CA N/A N/A Seilhamer; Jeffrey J. US-CL-CURRENT: 435/6,536/23.5 ,536/24.31

ABSTRACT:

The present invention provides nucleotide and amino acid sequences that identify and encode the hyaluronan receptor (hr) from human umbilical vein endothelial cells. The present invention also provides for antisense molecules

to the nucleotide sequences which encode hr, expression vectors for the production of purified HR, antibodies capable of binding specifically to HR, hybridization probes or oligonucleotides for detecting the upregulation of HR encoding nucleotide sequences, genetically engineered host cells for the expression of HR, diagnostic tests for activated, angiogenic, inflamed or metastatic cells and/or tissues based on HR-encoding nucleic acid molecules and

antibodies capable of binding specifically to the receptor.

#### CLAIMS:

We claim:

- 1. A method for detecting the presence of a polynucleotide comprising SEQ ID NO:1 in a sample containing nucleic acids, the method comprising the steps of:
- (a) contacting the nucleic acid of the sample with a polynucleotide having a sequence complementary to SEQ ID NO:1 under conditions suitable for formation of a double-stranded nucleic acid complex; and
- (b) detecting the presence of the complex, wherein the presence of the complex correlates with the presence of the polynucleotide comprising SEQ ID NO:1 in the sample.
- 2. The method of claim 1, further comprising the steps of:
- (a) analyzing the sample to determine the amount of complex present; and
- (b) comparing the amount of complex present to a standard value, whereby, if the amount of hybridization complex is larger than the standard value, the presence of inflammation or disease is indicated.

2 Claims, 2 Drawing figures Exemplary Claim Number: 1 Number of Drawing Sheets: 2 US-CL-CURRENT: 514/2,514/4 ,514/61

US-PAT-NO: 5902795

DOCUMENT-IDENTIFIER: US 5902795 A

TITLE: Oligosaccharides reactive with hyaluronan-binding protein and their

methods of use

DATE-ISSUED: May 11, 1999

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY Toole; Bryan P. Watertown MA N/A N/A Banerjee; Shib D. Melrose MA N/A N/A

US-CL-CURRENT: 514/54,514/2 ,514/4 ,514/61

ABSTRACT:

Hyaluronan-binding protein (HABP) is expressed on the cell surface during tumor cell and endothelial cell migration and during capillary-like tubule formation. Monoclonal antibodies and hyaluronan oligosaccharides are described

which specifically recognize HABP and can be used to (1) inhibit tumor growth by preventing tumor vascularization, (2) inhibit tumor cell migration and (3) image tumors.

## CLAIMS:

What is claimed is:

- 1. A method of inhibiting the growth of a tumor in a mammal, comprising administering an anti-tumor quantity of a hyaluronan oligosaccharide to the mammal having the tumor.
- 2. The method of claim 1, wherein said oligosaccharide is a tetradecasaccharide.
- 3. The method of claim 1, wherein said oligosaccharide is a hexasaccharide.
- 4. A method of inhibiting tumor metastasis in a mammal, comprising administering an anti-metastatic quantity of a hyaluronan oligosaccharide to the mammal having the tumor.
- 5. The method of claim 4, wherein said oligosaccharide is a tetradecasaccharide.
- 6. The method of claim 4, wherein said oligosaccharide is a hexasaccharide.
- 7. A pharmaceutical composition for treating a mammal afflicted with a tumor, comprising a hyaluronan oligosaccharide coupled to a cytotoxic agent.
- 8. The pharmaceutical composition of claim 7, wherein said hyaluronan

oligosaccharide is a tetradecasaccharide.

- 9. The pharmaceutical composition of claim 7, wherein said cytotoxic agent is methotrexate.
- 10. The pharmaceutical composition of claim 7, wherein said cytotoxic agent is diphtheria toxin.
- 11. A pharmaceutical composition for treating a mammal afflicted with a tumor, comprising a hyaluronan oligosaccharide coupled to a cytokine.
- 12. The pharmaceutical composition of claim 11, wherein said hyaluronan oligosaccharide is a tetradecasaccharide.
- 13. The pharmaceutical composition of claim 11, wherein said cytokine is selected from the group consisting of tumor necrosis factor, interferon and interleukin 2.
- 14. A method for treating a mammal afflicted with a tumor, comprising:
- a) excising the tumor from the body site;
- b) administering to the body site where the tumor was excised an anti-tumor quantity of a hyaluronan oligosaccharide.
- 15. The method of claim 14, wherein said oligosaccharide is a tetradecasaccharide.
- 16. The method of claim 14, wherein said anti-tumor quantity of said hyaluronan oligosaccharide is from about 50 .mu.g/ml to about 5 mg/ml.
- 17. The method of claim 14, wherein said oligosaccharide is a hexasaccharide.
- 18. A method of inhibiting growth of a tumor in a mammal, comprising administering to the mammal an anti-tumor quantity of a hyaluronan oligosaccharide wherein said oligosaccharide has between 1 and 16 disaccharide units.
- 19. The method of claim 18, wherein said oligosaccharide has between 3 and 7 disaccharide units.
- 20. The method of claim 18 wherein said tumor is a glioma or ovarian cancer.

- 21. A method of inhibiting growth of a tumor in a patient, comprising administering to the patient an anti-tumor quantity of a hyaluronan oligosaccharide.
- 22. The method of claim 21, wherein said oligosaccharide has between 1 and 16 disaccharide units.
- 23. The method of claim 21, wherein said oligosaccharide has between 3 and 7 disaccharide units.
- 24. The method of claim 21, wherein said oligosaccharide is a tetradecasaccharide.
- 25. The method of claim 21, wherein said oligosaccharide is a hexasaccharide.
- 26. A method of inhibiting tumor metastasis in a mammal, comprising administering to the mammal an anti-metastatic quantity of a hyaluronan oligosaccharide wherein said oligosaccharide has between 1 and 16 disaccharide units.
- 27. The method of claim 26, wherein said oligosaccharide has between 3 and 7 disaccharide units.
- 28. The method of claim 26 wherein said tumor is a glioma or ovarian cancer.
- 29. A method of inhibiting tumor metastasis in a patient, comprising administering to the patient an anti-metastatic quantity of a hyaluronan oligosaccharide.
- 30. The method of claim 29, wherein said oligosaccharide has between 1 and 16 disaccharide units.
- 31. The method of claim 29, wherein said oligosaccharide has between 3 and 7 disaccharide units.
- 32. The method of claim 29, wherein said oligosaccharide is a tetradecasaccharide.
- 33. The method of claim 29, wherein said oligosaccharide is a hexasaccharide.
- 34. A method for treating a mammal with a tumor, comprising:
- a) excising the tumor from the body site;

- b) administering to the mammal an anti-tumor quantity of a hyaluronan oligosaccharide wherein said oligosaccharide has between 1 and 16 disaccharide units.
- 35. The method of claim 34, wherein said oligosaccharide has between 3 and 7 disaccharide units.
- 36. The method of claim 34 wherein said tumor is a glioma or ovarian cancer.
- 37. A method for treating a patient a tumor, comprising:
- a) excising the tumor from the body site;
- b) administering to the patient an anti-tumor quantity of a hyaluronan oligosaccharide.
- 38. The method of claim 37, wherein said oligosaccharide has between 1 and 16 disaccharide units.
- 39. The method of claim 37, wherein said oligosaccharide has between 3 and 7 disaccharide units.
- 40. The method of claim 37, wherein said oligosaccharide is a tetradecasaccharide.
- 41. The method of claim 37, wherein said oligosaccharide is a hexasaccharide.
  41 Claims, 26 Drawing figures
  Exemplary Claim Number: 1
  Number of Drawing Sheets: 10

US-CL-CURRENT: 435/252.3,435/254.11 ,435/320.1 ,435/325 ,536/23.2

US-PAT-NO: 5827721

DOCUMENT-IDENTIFIER: US 5827721 A

TITLE: BH55 hyaluronidase DATE-ISSUED: October 27, 1998

INVENTOR-INFORMATION:

STATE ZIP CODE COUNTRY NAME N/A CA N/A Stern; Robert San Francisco CA N/A N/A Frost; Gregory I. San Francisco CA N/A N/A Hall; Jackson San Francisco San Francisco CA N/A N/A Shuster; Svetlana Colbern; Gail T. CA N/A N/A Pacifica Formby; Bent Santa Barbara CA N/A N/A

US-CL-CURRENT: 435/201,435/252.3 ,435/254.11 ,435/320.1 ,435/325 ,536/23.2

ABSTRACT:

The invention features a purified hyaluronidase BH55 polypeptide isolated from a mammalian species, preferably bovine or human. The invention also features DNA encoding BH55, vectors and transformed host cells containing DNA encoding BH55, methods of making BH55 hyaluronidase polypeptides, and antibodies that specifically bind BH55.

#### CLAIMS:

What is claimed is:

- 1. An isolated DNA molecule encoding bovine BH55 hyaluronidase.
- 2. An isolated DNA molecule, or degenerate variants thereof, encoding bovine BH55 hyaluronidase.
- 3. The DNA molecule of claim 1, wherein said DNA molecule is operably linked to regulatory sequences for expression of said BH55 hyaluronidase; and

wherein said regulatory sequences comprise a promoter.

- 4. A vector comprising the DNA molecule of claim 1.
- 5. A cultured transformed cell which contains the DNA molecule of claim 1.
- 6. A method of producing a BH55 hyaluronidase comprising:

culturing a cell transformed with a DNA molecule encoding a BH55 hyaluronidase under conditions for expressing said DNA molecule, said DNA molecule being positioned for expression in said cell; and

isolating said BH55 hyaluronidase.

- 7. The DNA molecule of claim 1, wherein the BH55 hyaluronidase comprises the amino acid sequence GPXPIYHIQEAVL (SEQ ID NO:1).
- 8. The DNA molecule of claim 1, wherein the BH55 hyaluronidase comprises the amino acid sequences  $\frac{1}{2}$
- a) Val-Leu-Xaa-Arg-Glu-Pro-Ala-Gly-Ala-Val-Ile-Xaa-Gly-Tyr-Gly-Thr-Pro-Arg-Ala-Thr-Val-Thr-Val-Thr-Leu-Xaa-Arg (SEQ ID NO: 2);
- b) Gly-Pro-Ser-Ala-His-Ser-Val-Leu (SEQ ID NO: 3);
- c) Met-Lys-Lys-Gly-Thr-Arg-Val-Lys-Xaa-Asp-Ser-Asn (SEQ ID NO: 4);
- d) Lys-Pro-Gly-Gly-Pro (SEQ ID NO: 5); and
- e) Xaa-Val-Phe-Gln-Val-Phe-Val-Ala-Xaa-Gly-Glu-Leu (SEQ ID NO: 6);

where Xaa represents any one of the twenty naturally-occurring amino acids. 8 Claims, 3 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 3

US-CL-CURRENT: 435/201,514/12 ,514/912

US-PAT-NO: 5747027

DOCUMENT-IDENTIFIER: US 5747027 A

TITLE: BH55 hyaluronidase DATE-ISSUED: May 5, 1998 INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Stern; Robert	San Francisco	CA	N/A	N/A
Frost; Gregory I.	San Francisco	CA	N/A	N/A
Hall; Jackson	San Francisco	CA	N/A	N/A
Shuster; Svetlana	San Francisco	CA	N/A	N/A
Formby; Bent	Santa Barbara	CA	N/A	N/A
Colbern; Gail T.	Pacifica	CA	N/A	N/A

US-CL-CURRENT: 424/94.62,435/201 ,514/12 ,514/912

**ABSTRACT:** 

The invention features a purified hyaluronidase BH55 polypeptide isolated from a mammalian species, preferably bovine or human. The invention also features DNA encoding BH55, vectors and transformed host cells containing DNA encoding BH55, the methods of making BH55 hyaluronidase polypeptides, and the antibodies that specifically bind BH55.

#### CLAIMS:

What is claimed is:

- 1. A bovine BH55 hyaluronidase having hyaluronic acid-specific .beta.-1,4-endoglycosidase activity, which hyaluronidase is free from the proteins and naturally occurring organic molecules with which it is naturally associated.
- 2. The hyaluronidase of claim 1, wherein said hyaluronidase contains the amino acid sequence GPXPIYHIQEAVL (Seq. ID No.: 1).
- 3. The hyaluronidase of claim 1, wherein said hyaluronidase has a molecular weight of about 55 kDa, as determined by 12.5% non-reducing SDS-polyacrylamide gel electrophoresis.
- 4. An injectable formulation comprising:
- a) a therapeutically effective amount of a bovine BH55 hyaluronidase, which hyaluronidase is free from the proteins and naturally occurring organic molecules with which it is naturally associated; and
- b) a pharmaceutically acceptable, injectable carrier.
- 5. The injectable formulation of claim 4, wherein the BH55 hyaluronidase

polypeptide is modified to effect an increase in serum half-life relative to the serum half-life of an unmodified BH55 hyaluronidase.

5 Claims, 3 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 3

US-CL-CURRENT: 435/252.3,435/254.11 ,435/320.1 ,435/325 ,536/23.5 ,536/24.31

US-PAT-NO: 5635370

DOCUMENT-IDENTIFIER: US 5635370 A

TITLE: DNA encoding BEHAB, a brain hyaluronan-binding protein, and

recombinant

expression systems for production of BEHAB polypeptides

DATE-ISSUED: June 3, 1997

INVENTOR-INFORMATION:

NAME CITY STATE ZIP CODE COUNTRY Hockfield; Susan North Haven CT N/A N/A Jaworski; Diane M. New Haven CT N/A N/A

US-CL-CURRENT: 435/69.1,435/252.3 ,435/254.11 ,435/320.1 ,435/325 ,536/23.5

,536/24.31 ABSTRACT:

A gene encoding mammalian brain enriched hyaluronan binding (BEHAB) protein is isolated and characterized from brain tissue and found to have a high

of sequence homology to members of the proteoglycan tandem repeat family of hyaluronan binding proteins. Unlike other members of the family, however, the expression of the gene is restricted to the central nervous system. BEHAB is expressed in markedly increased levels in human glioma tissue, so that the polypeptide can be used as a marker for diagnostic purposes.

#### CLAIMS:

# We claim:

- 1. An isolated nucleic acid molecule comprising a sequence selected from the group consisting of:
- (a) the sequence of a genomic DNA clone or a cDNA encoding a brain-enriched hyaluronan-binding (BEHAB) protein, wherein said DNA or cDNA is isolated from a

mammalian brain library, and wherein the noncoding strand of said DNA or cDNA hybridizes under stringent conditions with a DNA probe having the sequence shown as nucleotides 251 to 1363 of SEQ ID NO: 1 or the sequence shown as nucleotides 270 to 1403 of SEQ ID NO: 2;

- (b) a sequence degenerate with the sequence of (a); and
- (c) a sequence complementary to the full length of the nucleic acid of (a) or (b).
- 2. A nucleic acid molecule according to claim 1 which is DNA.
- 3. A nucleic acid molecule according to claim 1 which is RNA.

- 4. A nucleic acid molecule according to claim 1 which encodes a rat BEHAB protein.
- 5. A nucleic acid molecule according to claim 1 which encodes a cat  ${\tt BEHAB}$  protein.
- 6. A nucleic acid molecule according to claim 1 which encodes a human BEHAB protein.
- 7. A nucleic acid molecule according to claim 1 which is a cDNA.
- 8. A nucleic acid molecule according to claim 1 which is a genomic DNA clone.
- 9. An expression vector comprising the sequence of a nucleic acid molecule according to claim 1.
- 10. A host cell transformed or transfected with a nucleic acid according to claim  $1. \,$
- 11. A host cell transformed or transfected with an expression vector according to claim 9.
- 12. A process for preparing a mammalian BEHAB protein, comprising the steps of:

providing a host cell according to claim 10; and

culturing the host cell under conditions suitable for the expression of said nucleic acid.

13. A process for preparing a mammalian BEHAB protein, comprising the steps of:

providing a host cell according to claim 11; and

culturing the host cell under conditions suitable for the expression of said nucleic acid.

- 14. A process according to claim 12, further comprising the step of recovering said BEHAB protein.
- 15. A process according to claim 13, further comprising the step of

recovering said BEHAB protein.

- 16. An isolated DNA molecule comprising the sequence shown as nucleotides 251 to 1363 of SEQ ID NO: 1.
- 17. An isolated DNA molecule comprising the sequence shown as nucleotides 270 to 1403 of SEO ID NO: 2.
- 18. An isolated DNA molecule comprising the sequence shown as nucleotides 1 to 156 of SEQ ID NO: 7.
- 19. A vector comprising DNA having the sequence of a DNA molecule according to claim 16.
- 20. A vector comprising DNA having the sequence of a DNA molecule according to claim 17.
- 21. A vector comprising DNA having the sequence of a DNA molecule according to claim  $18. \,$
- 22. A host cell transformed or transfected with a vector according to claim 19.
- 23. A host cell transformed or transfected with a vector according to claim  $20. \,$
- 24. A host cell transformed or transfected with a vector according to claim 21.

24 Claims, 3 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 2